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Targeting expression of keratinocyte growth factor to keratinocytes elicits striking changes in epithelial differentiation in transgenic mice

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Keratinocyte growth factor (KGF) is a member of the fibroblast growth factor (FGF) family. Synthesized by cells of the dermal component of skin, KGF's potent mitogenic activity is on the epidermal component, which harbors the receptors for this factor. To explore the possible role of KGF in mesenchymal-epithelial interactions in skin, we used a human keratin 14 promoter to target expression of human KGF cDNA to the stratified squamous epithelia of transgenic mice. Mice expressing KGF in their epidermis typically appeared frail and weak, and often had grossly wrinkled skin. These mice exhibited a gross increase in epidermal thickness accompanied by alterations in epidermal growth and differentiation. Most remarkably, animals displayed several striking and unexpected changes, including a marked suppression of hair follicle morphogenesis and suppression of adipogenesis. With age, some animals developed gross transformations in the tongue epithelium and in epidermis. In addition, they exhibited elevated salivation and their salivary glands showed signs of altered differentiation. Collectively, our findings provide new and important insights into the roles of KGF, implicating this potent growth factor in eliciting global effects not only on growth, but also on development and differentiation, of skin and other tissues. In particular, KGF seems to interfere with signalling of some mesenchymal-epithelial interactions.

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